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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
HAYES, ROBERT CLINTON

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/21/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/357,273	Kaufman et al
Examiner	**Art Unit**
Robert C. Hayes, Ph.D.	1647

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 23, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above, claim(s) *6, 8-10, and 17-30* is/are withdrawn from consideration.

5) ☒ Claim(s) *1 and 2* is/are allowed.

6) ☒ Claim(s) *3-5, 7, and 11-16* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-30* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☒ The oath or declaration is objected to by the Examiner. - no citizenship provided.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I (claims 1-5, 7 & 11-16) in Paper No. 22 is acknowledged. It is again noted that claims 11-12 are incorrectly listed in Appendix A as being directed toward antibodies (versus claims 9-10), which are part of non-elected Group III.

Claims 28-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 22.

Allowable Subject Matter

2. Claims 1-2 are allowed.

Drawings

3. New formal drawings are required in this application because of the reasons indicated on PTO Form 948. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 U.S.C. § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 3-5 & 7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. For example, the current recitation of "a cell" encompasses a human organism. It is suggested that amending the claims to "an isolated host/transfected cell" should obviate this rejection.

5. Applicant is advised that should claim 13 be found allowable, claim 11 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Note further that claim 11 remains not incompliance with the Sequence Rules, in accordance with Paper No: 21, and will be held as nonresponsive to this Office action if not corrected; and if the AIPA Rules are not properly followed concerning amendments to the claims, as also indicated in Paper No: 21.

Claim Rejections - 35 U.S.C. § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11, 12, 13 & 14-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The sole written description provided within the specification is the human hlre1p sequence SEQ ID NO: 1 encoding SEQ ID NO:2 (e.g., Figs. 8 & 9; pg. 7). The specification, however, claims on pages 3 & 7 that hlre1p is "[a] novel polynucleotide peptide encoding a mammalian bifunctional protein kinase/endoribonuclease... [which] is expressed in the endoplasmic reticulum (ER) and upregulates the transcription of genes encoding ER protein chaperones...", based upon "34% identical at the amino acid level" with yeast Ire1p carboxy terminal domain and "37% identical to a *C. elegans* putative gene product having a similar domain organization sequence" at the "amino terminal half". However, not a single other "species homologue" of mammalian hlre1p is described; nor is a single "allelic variant of the polynucleotide" of SEQ ID NO:1 described. Moreover, no written description is provided in the instant specification as to what structurally constitutes broader heterologous encoded "proteins comprising fragments" thereof, or that encompass genomic nucleotide sequences that *comprise*

unknown and undescribed promoter sequences, 5'- or 3'-flanking or enhancer regions, introns or other sequences that "comprise" any polynucleotide "fragments" thereof, in which polynucleotide fragments further no longer constitute an open reading frame. In contrast, the mere presence of homologous regions from a yeast sequence does not in itself provide sufficient description of a representative number of species to show Applicants are in possession of the claimed genus; especially when the specification describes only the single "novel" human cDNA species of SEQ ID NO:1 (e.g., page 3 of the specification). Nor can one skilled in the art reasonably visualize or predict what critical encoded amino acid residues would structurally characterize the genus of polynucleotides encoding a "hlre1p" polypeptide, as currently claimed. Thus, the written description requirements under 35 U.S.C. 112, first paragraph are not met.

Secondly, although the specification describes expression vectors, which can be operably linked to the polynucleotide of SEQ ID NO:1, no generic "operatively linked... expression control sequence[s]", nor "hlre1p" promoter sequences, nor other genomic sequences that comprise an "expression control sequence" are adequately described within the specification that can be visualized by the skilled artisan; thereby, also not meeting the written description requirements under 35 U.S.C. 112, first paragraph, for claims 12 & 14-16.

Applicants are directed toward the Revised Interim Utility Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999.

7. Claims 11, 12, 13 & 14-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule encoding the human hlre1p polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for any structurally and functionally undefined hlre1p polynucleotides, or biologically functional equivalents thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The name, "nucleic acid molecule encoding hlre1p", alone (e.g., as defined on page 12 of the specification) encompasses any random mutation, "alteration, substitution, replacement, insertion or deletion", truncation, fragment or any biologically functional equivalent of any nucleic acid molecule encoding any hlre1p-related polypeptide, which provides little structural characterization and no functional characteristics for knowing how to make and use the instant invention. The specification further fails to define what specific encoded amino acids are critical for any hlre1p-related function, nor what nucleotide residues distinguish the nucleic acid of the instant invention from any nucleic acid encoding any different hlre1p-related protein. In contrast, the skilled artisan would reasonably expect that random mutations to any nucleic acid encoding the protein of SEQ ID NO:2 (i.e., as encompassed by the current claim language) would result in inactive encoded hlre1p-related proteins. For example, Rudinger states on page 3 that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different

positions of the same sequence". Rudinger then states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for an encoded hlre1p-related protein's function would prevent the skilled artisan from determining whether any random modification or mutation to a nucleic acid molecule that encodes a hlre1p-related protein could be made which retains the desired function of the instant invention, because any such random modification/mutation manifested within an encoded hlre1p-related polypeptide would be predicted to adversely affect the three-dimensional conformation of the encoded polypeptide, without requiring undue experimentation to determine otherwise.

Lastly, in that no expression sequences are contained in a structurally characterized DNA molecule, versus that expected with an expression vector comprising SEQ ID NO:1, the method of producing a hlre1p molecule would not reasonably work without requiring undue experimentation to determine what constitutes such "operatively linked... expression control sequence" (i.e., as it relates to claims 12 & 16).

8. Claims 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, base claim 13 has been amended to an "isolated polynucleotide"; thereby, no longer providing proper antecedent basis for "the host cell of Claim 13" in claims 14-16.

9. Claims 12 & 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what is exactly envisioned by the recitation of being "operatively linked to an expression control sequence", versus an expression vector comprising the polynucleotide of SEQ ID NO:1, etc., which reasonably would be operably linked to the expression *vector* control sequences, by definition. Additionally, no required vector sequences are recited in claim 11 for expressing "said polynucleotide", so that it can be subsequently "expressed", and then "isolated"; thereby, making claim 16 an incomplete method.

10. Claims 11-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what metes and bounds the recitation "having biological activity" is envisioned to entail, in that no specific assayable activity is recited in the claims.

Claim Rejections - 35 U.S.C. § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-13 & 15-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Mori et al. (IDS ref # C4; 1993).

Mori et al. teach a polynucleotide encoding an IRE1 protein "comprising a fragment of the amino acid sequence of SEQ ID NO:2" (i.e., residue #s 622-628; pg. 747; Fig. 4), which inherently has immunogenic "biological activity", etc. (i.e., as it relates to claims 11c & 13c). In that Mori's IRE1 polynucleotide meets the loosely defined limitations of both an "allelic variant" and "species homologue" of the polynucleotide of SEQ ID NO:1 (e.g., as defined on page 10 of the specification), claims 11d-e & 13d-e are also anticipated. In that Mori teach expression vectors/control sequences (e.g.., pSEYc102, pERN1EM, pMAL-c2, etc.), yeast and/or *E. coli* host cells, and a method of recombinantly producing their IRE1 polypeptide (e.g., pgs. 753-754), the limitations of claims 12 & 15-16 are also anticipated.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
April 15, 2003

GARY KUNZ
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